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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/019,494	03/08/2002	Samuel D. Bernal	344-P-29-CIP-USA	1407

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EXAMINER	
EBRAHIM, NABILA G	

ART UNIT	PAPER NUMBER
1618	

DATE MAILED: 06/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/019,494	BERNAL ET AL.	
	Examiner	Art Unit	
	Nabila G. Ebrahim	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 2* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 2* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/2/05 has been entered.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim recites a method for selective killing of epithelial cancer cells comprising the step of delivering to epithelial cancer cells a cationic supravital mitochondrial marking agent, the description of the phrase "supravital mitochondrial marking agent" in the instant specification is a cationic supravital mitochondrial marking agent, to cause cell death or to render the cancer cells substantially incapable of

multiplication. The marking agent can be delivered to the cancer cells in a single discrete dose, or continuously, or in repeated discrete doses, with or without employing a rinse reagent after each dose. The description is not complete since the Applicant did not describe precisely how the delivery of a non-toxic dye to the cancerous cells would kill the cells. In addition, Applicant did not describe or even suggest a dosage for using the dye as a cancer cell killer. In the mean time the examples offered by the Applicant for the method of selective killing –starting at example 6- provides using the dye with an adjuvant -("Adjuvant" as defined by instant specifications means a mitochondrial marking agent that, in combination with another chemotherapeutic agent, causes improved killing of cancer cells, either synergistically or by additive effects with the other agent)- or using the dye with and adduct (according to the instant specifications "Adduct" means the reaction product, either covalent or non-covalent, of a mitochondrial marking agent and a cancer chemotherapeutic agent.) Further, the applicant used toluidine blue in these examples, which is excluded by the claims.

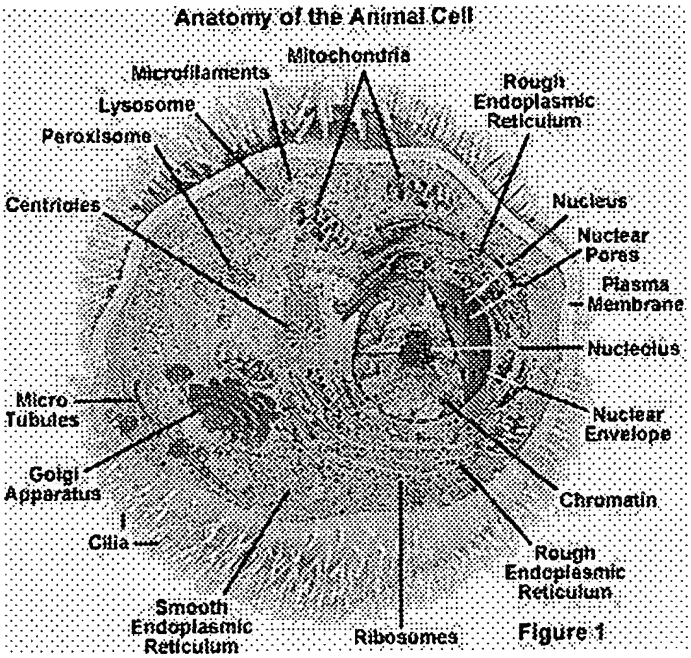
Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, and 2 rejected under 35 U.S.C. 102(b) as being anticipated by Pomerantz Edwin WO 9726018.

Pomerantz teaches in vivo detection of oral premalignant lesions and oral carcinomas, including the steps of sequentially rinsing the oral cavity with a dye stain composition which is selectively retained by cancerous and precancerous tissues, and a rinse composition for removing unretained stain composition, the step of applying to oral tissue, a stain composition comprising a non-toxic dye other than toluidine blue 0 (claim 1). Pomerantz also disclosed that this type of staining is dependent on the dye gaining access to internal subcellular structures such as the nucleus. Such access is readily obtained only by "fixing" a tissue sample of formaldehyde or other reagent that disrupts the cellular membrane without destroying general cellular structure (page 2, line 26 bridging to page 3, line 4). The disclosure of subcellular structures such as the nucleus includes mitochondria since both nucleus and mitochondria are subcellular structures enclosed within the cytoplasm (see figure below).



It is also known that the disclosure of oral carcinomas means oral malignancy of epithelial cells recited in instant claim 1.

In addition, Pomerantz teaches that in-vivo diagnostic procedures for detection of premalignant oral lesions or oral carcinomas, employing dye compositions, which are selectively retained by tissues rendered abnormal due to dysplasia, hyperplasia, tumorigenesis, and other active surface lesions, are known in the art.

Claim 2 is drawn to a method of selective killing of oral epithelial cancers cells comprising contacting the cancer cells with a cationic supravital mitochondrial-marking agent other than toluidine blue. Note that Pomerantz also excluded toluidine blue. Additionally, though instant application does not disclose the types of dyes used for the purpose of selective killing of the cancerous cells, the specification of the instant application discloses the use of Azure A and Azure B

for this purpose [0025] while in the mean time the prior art discloses the same dyes for selective detection of the cancerous cell (claim 2). Accordingly, since the prior art administered the same compound for the same population, it would inherently have the same effect on the cancerous cell because you can't separate between the compound and its properties.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, and 2 rejected under 35 U.S.C. 103(a) as being unpatentable over Pomerantz Edwin WO 9726018 in view of Hancock et al US 4816395.

Pomerantz has been discussed above. However Pomerantz does not disclose the use of Azure dyes as a method of therapy of oral epithelial cancerous cells.

As explained above claim 2 does not provide adequate written description of the compounds comprised in the cancerous cell method. However, for the purpose of examining the application the Examiner will consider the composition used comprising the dye other than toluidine blue and a chemotherapeutic as disclosed by the specifications.

Hancock teaches a method of both detecting and treating cancer cells comprising administering a cancer-marking agent, which is combined to a chemotherapeutic agent, (columns 2, and 3). The combination provides the ability of detecting the drug, which is naturally fluorescent or bound to a detectable label (claim 1).

It would have been obvious to a skilled artisan at the time the invention was made to modify the method disclosed by Pomerantz and use the same steps for treatment after combining a chemotherapeutic drug with the dye used for detection because Hancock disclosed that in case of epithelial cells treated with labelled methotrexate, the neoplastic cells which are not sensitive to the methotrexate will normally display a drug uptake which is at least 50% higher than that of normal mammary epithelial cells, usually being 300% higher, or more. The expected result would be a method of treating oral epithelial carcinomas.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claim 1 is rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 6649144. Although the conflicting claims are not identical, they are not patentably distinct from each other because the two claims recite the same invention except that claim 1 in '144 recites topically delivering the supervital mitochondrial marking agent. This does not differentiate the claim form instant claim 1 because instant claim 1 does not provide a method of administering the compound; it only gives a generic concept of administering the compound without limitations.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nabila G. Ebrahim whose telephone number is 571-272-8151. The examiner can normally be reached on 8:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nabila Ebrahim, M.D 5/24/06

MICHAEL G. HARTLEY
SUPERVISORY PATENT EXAMINER